

Appl. No. : 10/502,244
Filed : January 28, 2005

REMARKS

Claims 1-2 and 11 have been cancelled. Claims 3 and 6 have been amended. Claims 3-10 are now pending in this application. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 3-10 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action asserts that the use of the term “medicament” implies that the compound activity is known which is inconsistent with the screening method claimed. Claims 3 and 6 have been amended to remove the phrase “as a medicament”.

In view of Applicants’ amendment, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 1-6 are rejected under 35 U.S.C. § 102 (b) as anticipated by Majka, et al. and evidenced by Peichev, et al.

Majka, et al. teach AC133 as a marker for early human haematopoietic cells. Majka, et al do not teach anything regarding a role for AC133 in pathological angiogenesis. While malignant cells would be expected to display signs of pathological angiogenesis, Majka, et al. teach that AC133 is expressed in both normal and malignant cells and is undetectable on the majority of human solid tumor cells lines examined (see page 57, col. 2, last 6 lines). Therefore, there is no teaching in Majka, et al. which would lead one to use AC133 in a screen for molecules which could be used to treat pathological angiogenesis. The purpose of Majka, et al. is to evaluate AC133 as a marker for isolating early human haematopoietic progenitor cells (page 59, first paragraph of Discussion). Majka, et al. are silent on pathological angiogenesis.

The Examiner asserts that the haematopoietic cells of bone marrow are involved in angiogenesis and cites Peichev, et al. to evidence this assertion. However, Peichev, et al. merely teach that there is evidence for a population of CD34+ cells that coexpress AC133 and VEGFR-2 which have the capacity to migrate and differentiate into mature endothelial cells which supports

the existence of circulating endothelial precursors with the potential to contribute to postnatal angiogenesis (page 957, see last sentence). Yet, the mere presence of AC133 in these cells, alongside CD34 and VEGFR-2, and presumably numerous other proteins which were not subject to detection in that study, does not evidence that AC133 would be in itself involved in angiogenesis or that targeting AC133 would modulate angiogenesis. In fact, Peichev et al. admit that the function of AC133 is *unknown* (p. 953, col. 1, par. 4), which underscores the fact that they used AC133 merely as a cell marker, but disclosed nothing about the AC133's own biological function.

In contrast, the present application for the first time demonstrates that pathological angiogenesis is diminished in the absence of AC133. The present application shows that AC133 is not required for embryonic development and postnatal physiological vascular development, since these processes are normal in the AC133 knock out mouse (present specification, page 11, lines 14-20). Taken together this substantiates that compounds identified in the screening assays according to the present claims would selectively impair pathological angiogenesis, while not interfering with normal, physiological angiogenesis.

In summary, neither Majka, et al. nor Peichev, et al. teach a direct role for AC133 in angiogenesis. Neither Majka, et al. nor Peichev, et al. teach testing of molecules that bind to prominin-1 or to nucleic acids that encode prominin-1 as a treatment for pathological angiogenesis. Accordingly, the cited references do not teach all of the elements of the claimed invention.

In view of Applicants' arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 1-6 are rejected under 35 U.S.C. § 102 (b) as anticipated by Peichev, et al.

The disclosure of Peichev, et al. is directed to a small subpopulation of CD34+ cells which are VEGFR-2+ and AC133+. The authors suggest that such cells may play a role in neoangiogenesis (last sentence of Abstract). However, AC133 is merely disclosed as a marker for these cells. Yet, the mere presence of AC133 in these cells, alongside CD34 and VEGFR-2, and presumably numerous other proteins which were not subject to detection in that study, does not teach nor suggest that AC133 would be in itself involved in angiogenesis or that targeting

AC133 would modulate angiogenesis. In fact, Peichev et al. admit that the function of AC133 is *unknown* (p. 953, col. 1, par. 4), which underscores the fact that they used AC133 merely as a cell marker, but disclosed nothing about the AC133's own biological function.

While Peichev, et al. teaches that AC133+ is a marker for a particular subset of CD34+ cells, and that these cells may be involved in neoangiogenesis, there is no teaching that an agent that binds to AC133 or hybridizes to a nucleic acid encoding AC133 will be a potential medicament for the treatment of pathological angiogenesis. Peichev, et al. disclose binding of antibodies to AC133 merely to determine the number of AC133+ cells by FACS analysis. There is no recognition in Peichev, et al of the potential of AC133 to screen for agents that can be used to treat pathological angiogenesis. There is no teaching that drugs which bind to AC133 can be used to treat pathological angiogenesis. Peichev, et al. do not teach monitoring of pathological angiogenesis upon administration to a patient of molecules that either bind to prominin-1 (AC133) or to a nucleic acid encoding prominin-1 as claimed.

In contrast, the present application for the first time demonstrates that pathological angiogenesis is diminished in the absence of AC133. The application shows that AC133 is not required for embryonic development and postnatal physiological vascular development, since these processes are normal in the AC133 knock out mouse (page 11, lines 14-20). Taken together this substantiates that compounds identified in the screening assays according to the present claims would selectively impair pathological angiogenesis, while not interfering with normal, physiological angiogenesis.

In view of Applicants' arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 3-10 are rejected under U.S.C. § 103(a) as being unpatentable over Peichev, et al. and Majka, et al. in view of Babinet, et al. and in further view of Murphy, et al.

Peichev, et al. have been discussed above.

The Examiner asserts that Majka, et al. suggest using a knock out model to elucidate the role of AC133. While Majka, et al. do suggest the use of a knockout model to further characterize AC133, Majka, et al. neither teach nor suggest the use of a knockout model to screen for drugs that may be useful in the treatment of pathological angiogenesis. Furthermore, Majka,

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et al. also notes that receptor knockouts for AC133 have not yet been engineered (page 53, col. 2). Accordingly, Majka, et al. merely state that a knockout model for AC133 would be useful for further characterization of AC133, but does not speak to the screening method claimed by Applicants.

Babinet, et al. and Murphy, et al. are cited to teach knockout mice models. Murphy, et al. discloses a knockout mouse in which the FGF-19 gene has been inactivated. However, neither Babinet, et al. nor Murphy, et al. teach a knockout model for prominin-1 (AC133). Furthermore, neither Babinet, et al. nor Murphy, et al. teach or suggest a screening method for molecules effective against pathological angiogenesis. Accordingly, neither Babinet, et al. nor Murphy, et al. correct the deficiencies of Peichev, et al. and Majka, et al. discussed above.

In view of Applicants' arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

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Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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